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REMARKS

Upon entry of the amendments herein, claims 1-6, 8-20 and 24-37 remain pending in the application. Claims 1-6, 9, 10 and 34 have been amended herein; and claim 7 has been canceled.

Despite Applicants' arguments and the fact that the International Searching Authority found the claims to conform with the criteria for unity of invention, the Examiner has maintained the previous restriction requirement and made it final. Accordingly, claims 12-20, 24-31 and 35-37 currently stand withdrawn from consideration as being directed to nonelected subject matter; and claims 1-11 and 32-34 are presently being considered by the Examiner. Applicants comment further below on this situation.

In any event, it is expected, and respectfully requested, that upon determination of allowable subject matter in the elected claims and in accordance with U.S. practice, at least some of the nonelected subject matter will be rejoined and also allowed. More particularly, it is expected that at least some of the claimed subject matter directed to methods will be rejoined to the allowed composition-of-matter claims.

The Examiner has asserted that each of the 10 restriction groups "has a unique special technical feature that is different from each other," but has merely referred to the literal subject matter recited in the respective groups of claims without any explanation of how each of these alleged inventions is unique to the rest. In any case, Applicants wish to remind the Examiner that unity-of-invention criteria provide that a combination of claims directed to a product and claims directed to a method of using the product must be considered as a single invention. Further along these lines, the Examiner is reminded that neither

PCT Rule 13.2 nor MPEP §1850, invoked by the Examiner, limits unity of invention to claims directed to a single product and a single method of use. Thus, the fact that, for example, multiple products and multiple methods are recited in the present claims does not negate Applicants' entitlement to claims reciting the different categories (products and methods) of subject matter in a single application.

Applicants further wish to comment on the Examiner's citation of MPEP §1850 and her remarks with regard to Markush grouping and criteria (A), (B)(1) and (B)(2) of §1850(III)(B). The Examiner, in agreeing to examine all of the recited mutations together, asserts that it is criterion (B)(2) of MPEP §1850(III)(B) that is fulfilled in the present case. Applicants would disagree with this assessment in part. They would agree that the molecules containing the mutations of the present invention "belong to a recognized class of chemical compounds in the art to which the prior art pertains," but would not agree that the present case is one in which "the common structure cannot be the unifying criteria."

Applicants wish to make of record their belief that the present situation also meets criteria (A) and (B)(1) at least as well, if not better. Present claim 1 is directed to "[A]n isolated Nurrl gene, or a functional fragment or variant thereof..." [Emphasis added.] One of skill in the art would understand that in order for any fragment or variant to be functional, it would have to share a significant structural element with the parent gene. Accordingly, criterion (B)(1) of MPEP §1850(III)(B) is also fulfilled. Furthermore, as the Examiner herself has been willing to accept for the purpose of examination, "all alternatives have a common property or activity." Thus, criterion (A) is also fulfilled. Applicants wish to emphasize for the record that on all grounds, the

present claims must be considered to meet the criteria for unity of invention with respect to Markush practice.

Claims 9 and 33 stand rejected under 35 U.S.C. §101 as being directed to nonstatutory subject matter. These claims have been amended as suggested by the Examiner, and the rejection is moot.

Claims 1-11 and 32-34 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In general, the Examiner believes that the breadth of the claims is not warranted in view of the description provided in the specification.

In the first place, the Examiner asserts that the claimed genus "includes potentially a large number of nucleic acid sequences of various length and structure/sequences as long as it has a substitution of Met to Val, His to Arg, or a deletion of a Tyr." However, this assessment is incomplete. It must be emphasized that the members of the claimed genus must also have the same function, not just the one or more of the recited mutations. Hence, the breadth of the claims is considerably narrower than would be the case based on the Examiner's assessment.

Further along these lines, the Examiner states that the specification discloses three specific mutations in exon 3, which three do not include the deletion at position 121. Applicants wish to clarify that this is not a strictly accurate assessment, either. As disclosed on, for example, page 5, lines 21-25 of the specification, the invention encompasses all four of the mutations. Page 6, lines 12-15 provides the explanation that the mutations at positions 121 and 122 are indistinguishable from each other and that, therefore, the convention will be in the remainder of the disclosure to refer only to the mutation at position 122, even though the deletion

could occur at either position 121 or position 122. The two deletion mutations still must be considered as separate aspects of the invention, since the occurrence of either would yield the desired effects.

Moreover, the Examiner apparently believes that the claimed invention encompasses nucleic acid sequences which would encode proteins having sequences totally unrelated to the protein encoded by the Nurrl gene. However, this assertion is without any merit. From the language of the pending claims, anyone of skill in the art would certainly understand that the sequences encompassed by said claims are derived from the parent Nurrl gene and thus that it would not be possible for them to encode proteins having "totally unrelated sequences."

Still further, the Examiner asserts that it is not taught whether mutations at the same positions in the Nurrl gene from other species would produce the same effects or even whether the amino acids at positions 97, 103 and 122 are conserved in other species. In response, Applicants wish to call the Examiner's attention to U.S. Patent No. 7,037,657. From the Sequence Listing that is part of this patent, one can see that the four positions in question are conserved in the human, mouse and rat genes (see columns 137, 141 and 163 of the patent) and that even in the more evolutionarily distant species *Oryzias latipes* (Japanese killifish), two of the positions are conserved (see column 145).

Furthermore, particularly in view of the observed interspecies conservation at the positions in question, not to mention virtually 100% conservation of the entire sequences, one of skill in the art would certainly have reasonable expectation that the mutations of the present invention would exert the same effects on species other than human.

Finally in connection with the written description rejection, the Examiner singles out claim 7 because it recites a nucleic acid capable of specifically hybridizing to a gene or fragment according to claim 1. The cancellation of claim 7 by amendment herein renders moot this rejection. The cancellation is made without prejudice, and Applicants maintain the right to resume prosecution of the claimed subject matter in a continuation application.

For all of the reasons set forth above, the assessment that the specification does not meet the written description requirement is in error, and the rejection should be withdrawn.

Claims 1-11 and 32-34 also stand rejected under 35 U.S.C. §112, second paragraph as being indefinite because they recite nucleic acids with amino-acid mutations. The claims have been amended to achieve internal consistency, and this rejection is moot.

Claim 2 has further been rejected as being indefinite for reciting "the exons." The Examiner asserts that "it is unclear which exon applicant is referring to"; this assessment is also in error. This is not even a question of what would be appreciated by one of skill in the art, but rather what one of any skill level should appreciate simply from the universal meaning of the words. It must be emphasized that the claim does not recite "an exon" or "some of the exons." The term "the exons" found in present claim 2 would clearly be understood by anyone, whether skilled or not in the art, to include all of the exons of the gene. This rejection must also be withdrawn.

Finally, claim 7 stands rejected under 35 U.S.C. §102(b) as being anticipated by the article of Saucedo-Cardenas. The cancellation of the claim renders the rejection moot. Again, this cancellation is made without prejudice.

The specification passage running from page 5, line 21 through page 6, line 20 has been amended herein. This has been done to correct some inadvertent errors and in the interest of clarity. The changes made on page 6, lines 9-11 are clearly consistent with the intent of the invention found elsewhere throughout the application. The Examiner's attention is directed to, for example, page 9, lines 9-15; page 16, lines 11-16; and Figure 1. In fact, from a basic knowledge of the genetic code, the understanding of the convention by which the changes are expressed (e.g., "Met97Val"), and an inspection of Figure 1, it must be clear that the amendments made herein to page 6, lines 9-11 of the specification are necessarily correct. Thus, there can be no doubt that no new matter has been introduced. Entry of the amendments is respectfully requested.

In view of the arguments and amendments presented herein, all of the rejections under 35 U.S.C. §§101 and 112 have either been fully addressed or shown to be inappropriate in the first place. Furthermore, the invention as claimed is free of the cited prior art. Accordingly, the application is in condition for allowance. Reconsideration and allowance of the application with elected claims 1-6, 8-11 and 32-34 are respectfully requested. It is respectfully requested that at least some or all of the method claims be rejoined to the allowable composition claims and also allowed. Should any other matters require attention prior to allowance, it is requested that the Examiner contact the undersigned.

No fees should be due in connection with this communication. However, should it be determined that a fee is required for any reason, the Commissioner is hereby authorized to charge it to Deposit Account No. 23-1703.

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Respectfully submitted,



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